

### **DETAILED ACTION**

An amendment as received on 9/22/2011.

Claims 12-18, 27, 28, 31, and 34 were canceled, and claims 39-48 were added.

Claims 19-22, 29, 30, 32, 33, and 35-48 are pending and under consideration.

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mark DeLuca on 11/14/2011.

The application has been amended as follows:

#### **IN THE CLAIMS:**

In claims 19 and 32 delete "characterized by" and substitute --refers to-- therefor. This passage occurs in the fifth indented paragraph of section "C)ii)" of claim 19, and in the sixth paragraph of section "ii)" of claim 32.

In claim 22 insert --non-transitory-- immediately before "computer readable medium" in the first line of the claim.

Rewrite claim 29 as follows:

29. A method of preparing a microRNA that targets a selected mRNA sequence present in a cell, the method comprising:

confirming that a microRNA candidate oligonucleotide functions to inhibit expression of mRNA that comprises the selected mRNA sequence that is present in a cell, wherein the microRNA candidate is a nucleic acid molecule that has 17-25 nucleotides, has a sequence with complementarity to the selected mRNA sequence that is indicative of a microRNA to a microRNA recognition element, and has a sequence that when paired with the selected mRNA sequence has free energy of -20 kcal/mole or less, and inhibition of expression of mRNA that comprises the selected mRNA sequence in a cell by the microRNA candidate oligonucleotide is confirmed by:

contacting the microRNA candidate oligonucleotide with the mRNA that comprises the selected mRNA sequence that is present in the cell, and

determining expression of the mRNA that comprises the selected mRNA sequence in the cell;

wherein reduced expression of mRNA that comprises the selected mRNA sequence indicates that the microRNA candidate is a microRNA that targets the selected mRNA sequence; and,

wherein said microRNA candidate oligonucleotide is produced by a method comprising the steps of:

a) identifying the selected mRNA sequence of the mRNA that is present in the cell to be targeted by the microRNA candidate;

b) generating an oligonucleotide sequence that is a microRNA candidate sequence for targeting the selected mRNA, wherein said oligonucleotide

sequence is identified as a microRNA candidate sequence for targeting the selected mRNA using the system of claim 19, wherein:

the selected mRNA sequence to be the target of the microRNA is entered into said system using said input interface, and

said processor identifies a microRNA candidate sequence for targeting the selected mRNA sequence by performing said steps of said method of identifying a microRNA sequence that targets the selected mRNA sequence according to said programmed instructions;  
and

c) synthesizing a nucleic acid molecule comprising the nucleic acid sequence of the oligonucleotide sequence generated by said system and identified as a microRNA sequence that targets the selected mRNA, wherein said oligonucleotide sequence has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA-recognition element for a microRNA, and that has a sequence that when paired with the selected mRNA sequence was determined to have free energy of -20 kcal/mole or less, wherein the nucleic acid molecule comprises a microRNA candidate oligonucleotide.

Rewrite claim 35 as follows:

33. A method of preparing a microRNA that targets a selected mRNA sequence, wherein the microRNA that targets the selected mRNA sequence is a nucleic acid molecule that is 17-25 nucleotides, has a sequence with complementarity to the

selected mRNA sequence that is indicative of a microRNA to a microRNA recognition element and has a sequence that when paired with the selected mRNA sequence has free energy of  $-20$  kcal/mole or less,

the method comprising the steps of:

I) identifying a selected mRNA sequence to be the target of the microRNA;

II) generating an oligonucleotide sequence that is a microRNA sequence that targets the selected mRNA, wherein said oligonucleotide sequence is identified as a microRNA sequence that targets the selected mRNA using the system of claim 19, wherein:

the selected mRNA sequence to be the target of the microRNA is entered as input into said system at said input interface, and

said processor identifies a microRNA sequence that targets the selected mRNA sequence by performing said steps of said method of identifying a microRNA sequence that targets the selected mRNA sequence according to said programmed instructions;

III) synthesizing a nucleic acid molecule having the nucleic acid sequence of the oligonucleotide sequence generated by said system and identified as a microRNA sequence that targets the selected mRNA comprising the 17-25 nucleotide oligonucleotide sequence that has complementarity with the selected mRNA sequence that is indicative of a microRNA for a microRNA-response element and that has a sequence that pairs with selected mRNA sequence with a free energy determined to be  $-20$  kcal/mole or less,

wherein the nucleic acid molecule having the 17-25 nucleotide oligonucleotide sequence that has complementarity with the selected mRNA sequence that is indicative of a microRNA for a microRNA-response element and that has a sequence that when paired with the selected mRNA sequence has free energy determined to be -20 kcal/mole or less is a microRNA that targets the selected mRNA sequence.

In claim 35 delete "IV" and substitute --III-- therefor.

### ***Reasons for Allowance***

The following is an examiner's statement of reasons for allowance: The Examiner's amendment to claim 19 overcomes the grounds of rejection under 35 USC 101. The amendments to claims 29 and 33, incorporating the use of the system of claim 19 as a method step, overcome the prior art rejections of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

### ***Information Disclosure Statement***

An information Disclosure Statement was filed on 7/23/2007, and was signed, initialed, and dated by an Examiner on 8/11/09. This Action contains a corrected

version of he signed, initialed, and dated IDS in which the year of publication has been added to reference BP on page 4 off 6.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Heather Calamita, can be reached at (571) 272-2876. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Richard Schnizer/  
Primary Examiner, Art Unit 1635